

(5AΔ47)}, containing the NS5A adaptive mutations, S2204I and an in-frame deletion of 47 amino acids (Δ47aa) between nt 6960 and 7102, respectively, have been described (5) (Fig. 1). The plasmid pHCVBMFL/S2204I {FL (S2204I); Fig. 1} contains the full-length genome with the NS5A adaptive change S2204I. For the genomic and subgenomic constructs, NS5B polymerase defective derivatives were generated carrying a triple amino acid substitution, changing the Gly-Asp-Asp (GDD) motif in the active site to Ala-Ala-Gly (AAG) (5), and throughout this report are referred to as pol-.

Please replace the paragraph on page 12, lines <sup>2</sup>~~1~~-15 of the specification as originally filed with the following paragraph amended as indicated below:

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Total cellular RNA was isolated using TRIzol reagent (Gibco-BRL) according to the manufacturer's protocol. One-tenth of each RNA sample was used to quantify HCV-specific RNA levels using an ABI PRISM 7700 Sequence Detector (Applied Biosystems). Real time reverse transcription (RT)-PCR amplifications were performed using the TaqMan EZ RT-PCR core reagents (Applied Biosystems) and primers specific for the HCV 5' NTR: 5'-CCTCTAGAGCCATAGTGGTCT-3' (SEQ ID NO: 1) (sense, 50 μM), 5'-CCAAATCTCCAGGCATTGAGC-3' (SEQ ID NO: 2) (antisense, 50 μM) and FAM-CACCGGAATTGCCAGGACGACCGG (SEQ ID NO: 3) probe, 10 μM; (Applied Biosystems). RT reactions were incubated for 30 min at 60°C, followed by inactivation of the reverse transcriptase coupled with activation of *Taq* polymerase for 7 min at 95°C. Forty cycles of PCR were performed with cycling conditions of 15 sec at 95°C and 1 min at 60°C. Synthetic HCV